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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,259	10/31/2003	Beth P. Nguyen	PROTEO.P08CI	7361

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EXAMINER	
KOLKER, DANIEL E	

ART UNIT	PAPER NUMBER
1649	

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08/20/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/698,259	NGUYEN ET AL.	
	Examiner	Art Unit	
	DANIEL KOLKER	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10 and 33-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10,33-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks and amendments filed 21 April 2008 have been entered. Claims 1 – 8, 10, and 33 – 35 are pending and under examination.

Maintained Rejections and Objections

Priority

2. The effective filing date of claims 1 – 8 and 10 is 1 November 2002; the effective filing date for claims 33 – 35 is 31 October 2003 for the reasons set forth in the office action mailed 21 December 2007. Applicant did not traverse the examiner's determination that these are the appropriate effective filing dates.

Double Patenting

3. Claims 1 – 8, 10, and 33 – 35 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 4, 6 – 9, 14 – 15, and 19 – 21 of U.S. Patent No. 7,148,001. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in the parent application do not require that the GAGs be immobilized. However this very minor modification would have been obvious to one of ordinary skill in the art as immobilizing the GAGs would allow for rapid separation of the A-beta fibrils from the GAGs after the fibrils had formed. The newly-added limitations in claims 1 and 10 are not sufficient to overcome the double-patenting rejection of record. The claims have been amended to methods of inducing "particular amyloid plaques", this is recited in claims 1 and 6 of the '001 patent for example. The claims also require that a Maltese-cross pattern be formed, again this is recited in claims 1 and 6 of the '001 patent.

Applicant did not traverse the rejection but rather stated that a terminal disclaimer may be filed in the future. No such disclaimer has been filed, so the rejection stands for the reasons of record.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 – 7 and 33 – 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Castillo (1997. Journal of Neurochemistry 69:2452-2465) in view of Hornbeck (1991. Current Protocols in Molecular Biology 11.2.1 - 11.2.22) and Grainger (U.S. Patent 6,395,494, issued 28 May 2002, filed 7 June 1995).

This rejection stands for the reasons previously made of record. The reasons why every claim limitation is met or suggested by the prior art references have been set forth in the office action mailed 21 December 2007 and will not be repeated herein. Briefly, Castillo teaches methods comprising immobilizing the sulfated gylcosaminoglycan (SGAG) on a selected medium, and adding the Aβ which is known to be fibrillar, to the medium. The assay is akin to an ELISA, although it relies upon the interaction between Aβ and perlecan rather than between an antibody and it antigen. As set forth in the office action mailed 20 November 2006, the Aβ and SGAG are in a 1:1 ratio. Castillo teaches that the medium is a titer well plate (p. 2454, first paragraph), as recited in claim 6. Finally, Castillo teaches that perlecan is a heparan sulfate (see abstract, first sentence; see also p. 2453 first paragraph), as recited in claim 7. However Castillo does not explicitly teach the step of air-drying the SGAG on the medium, as recited in claim 1.

Hornbeck teaches that the ELISA is a well-known assay format useful to detect the amount of a specific reagent in a solution. Hornbeck teaches that the method relies on antibody-antigen interaction, wherein an antibody specifically binds to its cognate antigen. Hornbeck teaches several types of ELISA, and specifically teaches that in all types of the assay the first reagent (usually an antigen) is adsorbed onto a solid surface, and then solutions

containing the compound to be analyzed are usually added. Finally, a detecting step is performed to determine how much of the compound is present and bound to the adsorbed antigen. Hornbeck teaches that the step of immobilizing the first product on the substrate can be performed at 4°C or at 37°C, and can be done between 2 hours to "overnight" (i.e., about 16 hours); see p. 11.2.4 first paragraph. However Hornbeck does not explicitly teach drying the first product on to the substrate as part of the immobilizing process, and does not teach either Aβ or SGAG, as recited in claim 1.

Grainger teaches an ELISA method to detect the amount of specific TGF-β in solution. The assay involves the step of coating the microtiter wells with the first antigen (in this case, an antibody), and allowing the antigen (here, an antibody) to dry by evaporation at room temperature, which Grainger teaches is about 12 hours (see column 48 lines 45 - 48). This is on point to the limitation "allowing SGAG to air dry on the selected medium" recited in claim 1. Grainger teaches that following subsequent washing steps, the solution containing the substance to be analyzed is added, and then detected with detection antibodies, horseradish peroxidase, and a chromogen. While Grainger does not specifically teach the temperature at which the assay was performed, it is reasonable that it was performed at room temperature, which is about 25 °C and therefore on point to claim 33. However Grainger does not teach either Aβ or SGAG, as recited in claim 1.

It would have been obvious to one of ordinary skill in the art to modify the method of Castillo to include the step of allowing the first product to air dry, as taught by Grainger, with a reasonable expectation of success. The motivation to do so would be to develop an accurate and reliable ELISA-type assay for quantitating the amount of Aβ in a sample. Allowing the product to air dry would be advantageous, as it would assure that all of the first reagent (in this case, the SGAG perlecan) would be immobilized onto the substrate. The skilled artisan would have been motivated to take this step, as Castillo teaches that only about 20% of perlecan is immobilized on a mirotiter well. Thus by performing this step, the artisan would reasonably expect to have more perlecan immobilized, thereby allowing for a greater range of detection in the assay. The examiner has included claims 34 and 35 in this rejection as well. While none of the references explicitly teaches the exact time or temperature recited in these claims, optimizing an assay is within the skill of the ordinary artisan. Additionally, the reference by Hornbeck teaches that the second step, i.e. when the two binding compounds are contacted, should take place "≥ 2 hr at room temperature." (p. 11.2.4, step 8), providing guidance to the

artisan as to the lower bound of time that should be used. Selection of a point within this range (i.e. 12 to 24 hours as recited in claim 35) does not constitute a patentable contribution; see MPEP § 2144.05(II). Additionally, selection of 37 °C, recited in claim 34, would have been obvious to one of ordinary skill in the art as this is physiological temperature in mammals, and thus least likely to have deleterious conformation-altering effects on the protein used in the assay, and is explicitly taught as a suitable assay temperature by Hornbeck.

Applicant did not traverse the examiner's determination that the specific steps and starting materials recited in the claims would have been obvious to one of ordinary skill in the art. Rather applicant argued that the newly-added limitations to independent claims 1 and 10 distinguish the claimed invention from the prior art references. The examiner acknowledges that none of the references explicitly teaches that Maltese cross patterns are formed by the method that is rendered obvious by the cited prior art references. This limitation is explicitly recited in independent claims 1 and 10. However, this is not an additional step, and requires no additional starting materials. Rather, this newly-added limitation is a reference to something that will necessarily occur upon performing this method. Absent evidence to the contrary, it is presumed that the plaques that are formed will be spherical and will demonstrate a Maltese cross pattern when stained with Congo Red and viewed under polarized light. The claim, as written, does not require the step of staining with Congo Red, and does not require the step of viewing plaques under polarized light. The prior art renders obvious the claimed starting materials and method steps, so inclusion of the claims in this rejection even though the references are silent as to this property which appears to be inherent; see MPEP § 2112(III). Note that U.S. Patent 7,148,001 (Castillo) provides evidence that incubating β-amyloid and heparan sulfate together induces the formation of spherical plaques that form Maltese cross patterns when viewed under polarized light (see for example claim 1).

5. Claims 1 – 8 and 33 – 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Castillo in view of Hornbeck and Grainger as applied to claims 1 – 7 above, and further in view of Cross (1989. Journal of Tissue Culture Methods 12:57-59, of record).

This rejection stands for the reasons of record. The reasons why claims 1 – 7 and 33 – 35 are obvious over Castillo in view of Hornbeck and Grainger are set forth above. However none of the references teaches 96-well Teflon coated slides as encompassed by claim 8.

As set forth previously, Cross teaches a 96-well Teflon-coated partitioned block, which could reasonably be called a "slide", since the low friction of Teflon allows it to slide easily. Note that claim 8 sets no restrictions on the size of the so-called slide. Cross teaches that the 96-well Teflon plate is advantageous as it is compatible with both non-polar and polar solvents, and it can be sterilized and re-used. Furthermore the 96-well format is convenient for making dilutions. However Cross does not teach methods of inducing amyloid plaques as recited in claim 1.

It would have been obvious to one of ordinary skill in the art to use a 96-well Teflon slide, as taught by Cross, in the method rendered obvious by Castillo in view of Hornbeck and Grainger. The motivation to do so would be to use a format that is convenient to researchers, namely the 96-well format. Furthermore Cross teaches that the Teflon-partitioned slide is advantageous as it can be re-sterilized, thereby decreasing waste and cost. Applicant did not traverse the examiner's determination that the specific limitations of claim 8 would have been obvious in view of Cross, but argued that independent claim 1 is not obvious in view of the newly-added limitation. For the reasons set forth above, the invention of claim 1 is obvious, thus this rejection of claims 1 – 8 and 33 – 35 stands.

6. Claims 1 – 8, 10, and 33 – 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Castillo in view of Hornbeck, Grainger, and Cross as applied to claims 1 – 8 and 33 – 35 above, and further in view of Roach (U.S. Patent 3,494,201, issued 10 February 1970, of record).

This rejection stands for the reasons previous made of record. The reasons why claims 1 – 8 and 33 – 35 are rendered obvious are set forth in the previous rejections. However none of the references explicitly teaches "bubbling" as recited in claim 10.

Roach teaches pipetters which use air to displace a liquid contained within the pipetter. Roach also teaches that pressing the dispensing shaft beyond the set-point for drawing up liquid to ensure that all liquid is released (see for example column 4). The artisan of ordinary skill would have the experience to understand that when pipetting, bubbles are frequently released into the solution. This is an indication that all the solution contained within the pipet tip has left the tip and has been released into the recipient solution.

It would have been obvious to one of ordinary skill in the art to use a bubbling technique in performing the assay rendered obvious by Castillo in view of Hornbeck, Grainger, and Cross.

The motivation to do so would be to ensure that all liquid from the pipet tip had been forced out; an air bubble would be a reliable indicator that this had been accomplished. Applicant did not traverse the examiner's determination that the specific limitations of claim 10 would have been obvious in view of Roach, but argued that independent claim 1 is not obvious in view of the newly-added limitation. For the reasons set forth above, the invention of claim 1 is obvious, thus this rejection of claims 1 – 8, 10 and 33 – 35 stands.

Conclusion

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANIEL KOLKER whose telephone number is (571)272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel E. Kolker, Ph.D./
Patent Examiner, Art Unit 1649
August 15, 2008